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REMARKS

Claims 8, 10, 11, 16, 26, 28, 29 and 37-48 were pending in the application. Claims 8, 16, 26, 37, and 44 have been amended. New claims 49-51 have been added. Accordingly, claims 8, 10, 11, 16, 26, 28, 29 and 37-51 are now pending.

Support for the amendment to claims 8 and 26 and new claim 49 can be found in Figure 9. Additional support for new claim 49 can be found throughout the specification, including at least at page 22, lines 6-12 and in Figures 11 and 12. Support for new claims 50 and 51 can be found in the specification at page 18, lines 28-30 and in Table II. No new matter has been added.

Amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and were done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Interview Summary

Applicants acknowledge and thank the Examiner for the telephone interview with Applicants' attorney on July 26, 2005. In particular, Applicants' attorney and the Examiner discussed the claim language in view of the art cited by the Examiner in the final Office Action dated December 28, 2004. Possible claim amendments were discussed and are provided herewith for the Examiner's review.

Rejection of Claims 8, 10, 26-28, 39, 40, and 42 Under 35 U.S.C. §102(b) in view of Crowe *et al.*, Rennert *et al.*, and Kwon *et al.*

The Examiner has rejected claims 8, 10, 26-28, 39, 40, and 42 as being anticipated by Crowe *et al.* (1994) *Science* 264:707 (hereinafter Crowe-Science); claims 8, 11, 26, 29, 37-40, and 42 as being anticipated by Kwon *et al.* (1997) *J. Biol. Chem.* 272:14272 (hereinafter Kwon); and claims 8, 10, 16, 26, 28, and 39-42 as being anticipated by Rennert *et al.* (1996) *J. Exp. Med.* 184:1999 (hereinafter Rennert). The Examiner maintains that "the process of

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making the product in this case does not impart any structurally distinct characteristics that would help distinguish this product over that of the prior art." Applicants respectfully traverse this rejection in view of the arguments presented in the Amendment and Response filed on May 31, 2005 and those described in detail below.

Under 35 U.S.C. 102, for a prior art reference to anticipate a claimed invention, the prior art must teach *each and every element* of the claimed invention. *Lewmar Marine v. Barent*, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987). Furthermore, "the identical invention must be shown in as complete detail as is contained in the...claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Applicants respectfully submit that the Examiner has failed to establish how any of the cited references teaches each and every element of the claimed invention in accordance with 35 U.S.C. §102. Furthermore, the claimed invention has improved ligand binding activity over the products taught in the cited references, described in more detail below.

The claimed invention is directed to a *high yield preparation enriched in biologically active receptor-Ig protein* comprising a high yield percentage of biologically active TNF family receptor-Ig-fusion protein, *e.g.*, at least 70%, and/or a low percentage of inactive receptor-Ig fusion protein, *e.g.*, no more than 30%, obtained by culturing a host cell in a culture system having a reduced temperature relative to the conventional temperatures known in the art. In addition, new claim 49 is directed to a highly enriched cell culture supernatant obtained by culturing a mammalian host cell transformed with DNA encoding a receptor-Ig fusion protein in a culture system having a temperature of about 27° C to about 35° C comprising

- a) at least 70% biologically active receptor-Ig-fusion protein; and
- b) no more than 30% inactive receptor-Ig fusion protein,

wherein the receptor-Ig fusion protein comprises a member of the TNF family of receptors and the *supernatant has improved ligand binding relative to a high temperature supernatant* obtained by culturing a mammalian host cell transformed with DNA encoding the receptor-Ig fusion protein in a culture system having a temperature greater than about 35° C.

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The claimed invention has improved properties over the preparations described in the cited art since the claimed preparations and cell culture supernatants are highly enriched for biologically active TNF receptor-Ig fusion proteins due to Applicants' low temperature culturing method. As described in the instant specification at page 22, lines 6-15 and in Figures 11 and 12, Applicants provide experimental results which demonstrate that a preparation comprising TNF family receptor-Ig fusion proteins cultured at a temperature lower has improved binding to the ligand in comparison to a preparation cultured at 37° C. The specification describes experiments which examine the binding properties of preparations comprising HVEM-Ig fusion proteins using FACS binding assays and BLAcore chip analysis to determine the binding properties of preparations cultured at various temperatures, including the conventional temperature of 37° C and low culture temperatures of 32° C and 28° C. As shown in Figure 11, FACS analysis of cells from cultures grown at 37° C and 32° C demonstrate that the "ability of HVEM-Ig to bind cell surface ligand was improved roughly 2-3 fold upon expression at 32° C" (see description in specification at page 8, lines 4-10 and page 22, lines 6-8). In addition, BLAcore analysis of preparations produced at 32° C and 28° C demonstrate that ligand binding was improved in comparison to preparations produced at 37° C (see Figure 12). As described in Applicants' Amendment and Response filed May 31, 2005, each of the references cited by the Examiner culture host cells expressing the receptor-Ig fusion proteins at the conventional temperature of 37° C. Thus, in view of the improved binding activity of preparations cultured at temperatures lower than 37° C, Applicants submit that the claimed invention is novel over Crowe-Science, Rennert, and Kwon. Applicants respectfully request that the rejection under 102(b) in view of Crowe-Science, Rennert, and Kwon be reconsidered and withdrawn.

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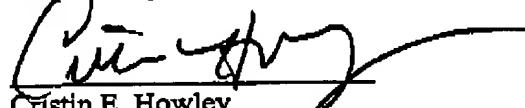
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CONCLUSION

Amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. In view of the foregoing amendments, reconsideration of the rejections and allowance of all pending claims is respectfully requested. The amendments made to the claims are not related to any issues of patentability.

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the examiner is urged to call Applicants' Attorney at (617) 227-7400.

Respectfully submitted,



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Dated: August 2, 2005